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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040405

Application Number: 09/966,893
Filing Date: September 28, 2001
Appellant(s): D'AZZO ET AL.

James Scott Elmer
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 10, 20003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Sharp. WO 00/31950

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

35 U.S.C. § 112, 1st Paragraph - Written Description

Claims 8-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 8 is genus claim that is directed toward any pharmaceutical composition comprising any pharmaceutically acceptable carrier and any protein of any structure and function useful for treating any lysosomal storage disorder other than Fabry disease, wherein the claimed protein is selectively imported into macrophages when administered to a subject and the protein is produced in any insect cell. Claims 11 and 12 which depend from the genus claim 8 limit the genus to the specific insect cell of *Spodoptera frugiperda* or *Tricoplusia ni*. Claim 13 which depends from the genus claim 8 limits the genus where the claimed protein is produced in cell culture using a baculovirus expression system.

Claim 9 which depends from claim 8 is a genus claim that is directed toward any pharmaceutical composition comprising any pharmaceutically acceptable carrier and any protein of any structure and function useful for treating galactosialidosis, wherein the claimed protein is selectively imported into macrophages when administered to a subject and the protein is produced in any insect cell.

Claim 10 which depends from claim 8 is genus claim that is directed toward any pharmaceutical composition comprising any pharmaceutically acceptable carrier and

any protective protein/cathepsin A (PPCA) protein of any structure and amino acid sequence useful for treating any lysosomal storage disorder other than Fabry disease, wherein the claimed protein is selectively imported into macrophages when administered to a subject and the protein is produced in any insect cell.

The scope of genus claim 8 includes many proteins with widely differing structural, chemical, and physical characteristics, and the genus is highly variable because a significant number of structural differences between protein genus members is permitted. Furthermore, the scope of genus claim 8 includes many widely differing lysosomal storage disorders that have widely differing etiologies based on their respective enzyme and/or protein deficiencies (see Table 1 on pages 3-6 of the specification).

The scope of genus claim 9 includes many proteins useful for treating galactosialidosis where the proteins have widely differing structural, chemical, and physical characteristics, and the genus is highly variable because a significant number of structural differences between protein genus members is permitted.

The scope of genus claim 10 includes many PPCA proteins with widely differing structural, chemical, and physical characteristics, and the genus is highly variable because a significant number of structural differences between PPCA protein genus members is permitted. Furthermore, the scope of genus claim 10 includes many widely differing lysosomal storage disorders that have widely differing etiologies based on their respective enzyme and/or protein deficiencies.

Example 1 of the specification describes uptake experiments where baculovirus-expressed neuraminidase and baculovirus-expressed PPCA (BV-neur and BV-PPCA, respectively), either alone or mixed, were taken up by PPCA-deficient mouse macrophages resulting in the restoration of cathepsin A and neuraminidase activities in the PPCA-deficient mouse macrophages (see p. 19, line 21 to p. 20, line 12).

Example 1 of the specification further describes the administration of BV-neur and BV-PPCA to PPCA-deficient mice over a two week period resulting in a significant increase in the cathepsin A and neuraminidase activities in several systemic organs and the presence of PPCA in macrophages. However, the specification does not provide the specific amino acid sequence and structure of the BV-neur and BV-PPCA protein.

The specification fails to provide additional representative proteins useful for treating any lysosomal storage disorder encompassed by the genus claims 8, 9, and 10 other than the BV-neur and BV-PPCA described in Example 1 which was taken up by PPCA-deficient mouse macrophages and used to treat PPCA-deficient mice. The specification does not provide a written description of any pharmaceutical composition comprising any protein that can be used to treat any lysosomal storage disorder.

Given this lack of additional representative proteins as encompassed by the claims, Appellants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Appellants were in possession of the claimed invention. Claims 11-13 which depend from claim 8 are also rejected because they do not correct the defect of claim 8.

35 U.S.C. § 112, 1st Paragraph - Enablement

Claims 8-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for composition comprising a protective protein/cathepsin A (PPCA) protein useful for treating galactosialidosis, does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of claim 8 encompasses any pharmaceutical composition comprising any pharmaceutically acceptable carrier and any protein of any structure and function useful for treating any lysosomal storage disorder other than Fabry disease, wherein the claimed protein is selectively imported into macrophages when administered to a subject and the protein is produced in any insect cell. The scope of claim 8 includes many proteins with widely differing structural, chemical, and physical characteristics and many widely differing lysosomal storage disorders that have widely differing etiologies based on their respective enzyme and/or protein deficiencies

(see Table 1 on pages 3-6 of the specification). Claims 11 and 12 which depend from the claim 8 limits the claim to the specific insect cell of *Spodoptera frugiperda* or *Tricoplusia ni*. Claim 13 which depends from the claim 8 limits claim 8 where the claimed protein is produced in cell culture using a baculovirus expression system.

The nature and breadth of claim 9 encompasses any pharmaceutical composition comprising any pharmaceutically acceptable carrier and any protein of any structure and function useful for treating galactosialidosis, wherein the claimed protein is selectively imported into macrophages when administered to a subject and the protein is produced in any insect cell. The scope of claim 9 includes many proteins useful for treating galactosialidosis where the proteins have widely differing structural, chemical, and physical characteristics.

The nature and breadth of claim 10 encompasses any pharmaceutical composition comprising any pharmaceutically acceptable carrier and any protective protein/cathepsin A (PPCA) protein of any structure and amino acid sequence useful for treating any lysosomal storage disorder other than Fabry disease, wherein the claimed protein is selectively imported into macrophages when administered to a subject and the protein is produced in any insect cell. The scope of claim 10 includes many PPCA proteins and allelic variants of PPCA proteins with widely differing structural, chemical, and physical characteristics and many widely differing lysosomal storage disorders that have widely differing etiologies based on their respective enzyme and/or protein deficiencies.

The specification provides guidance and examples for injecting a baculovirus expressed and purified neuraminidase and PPCA into PPCA-deficient macrophages and PPCA-deficient mice. Example 1 of the specification describes uptake experiments where baculovirus-expressed neuraminidase and baculovirus-expressed PPCA (BV-neur and BV-PPCA, respectively), either alone or mixed, were taken up by PPCA-deficient mouse macrophages resulting in the restoration of cathepsin A and neuraminidase activities in the PPCA-deficient mouse macrophages (see p. 19, line 21 to p. 20, line 12). Example 1 of the specification further describes the administration of BV-neur and BV-PPCA to PPCA-deficient mice over a two week period resulting in a significant increase in the cathepsin A and neuraminidase activities in several systemic organs and the presence of PPCA in macrophages. However, the specification does not provide the specific amino acid sequence and structure of the BV-neur and BV-PPCA protein.

While molecular biological techniques and genetic manipulation techniques are known in the prior art and the skill of the artisan are well developed, knowledge regarding whether any pharmaceutical composition comprising any protein of any structure and function can be used to treat any patient having any lysosomal storage disorder as encompassed by claim 8 without harming the patient is lacking.

Knowledge regarding whether any pharmaceutical composition comprising any protein of any structure and function can be used to treat any patient having galactosialidosis as encompassed by claim 9 without harming the patient is lacking.

Knowledge regarding whether any pharmaceutical composition comprising any PPCA protein can be used to treat any patient having any lysosomal storage disorder as encompassed by claim 10 without harming the patient is lacking.

It cannot be predicted whether any protein of any structure and function can be used to treat any patient having any lysosomal storage disorder without any harming the patient. The specification does not disclose any other examples of any other protein that is shown and demonstrated to be useful to treat any other lysosomal storage disorder other than the BV-neur and BV-PPCA used in Example 1 of the specification. Instead the specification simply states in p. 14, line 30 to p. 15, line 10, how a subject suffering from sialidosis or GM1-gangliosidosis may be treated by administration of neuraminidase or beta-galactosidase, respectively. No information is provided which demonstrates that a subject suffering from sialidosis or GM1-gangliosidosis is successfully treated with neuraminidase or beta-galactosidase.

The amount of experimentation to search for any pharmaceutical composition comprising any polypeptide of any structure and function which can be used to treat any patient having any lysosomal storage disorder as encompassed by claim 8 without harming the patient is enormous and undue. Such experimentation entails determining whether a particular disease is a lysosomal storage disorder disease, determining the etiology of the disease, searching and screening for any protein of any structure and function, and determining whether any pharmaceutical composition comprising the

protein would be useful in treating the patient having any lysosomal storage disorder without harming the patient.

The amount of experimentation to search for any pharmaceutical composition comprising any polypeptide of any structure and function which can be used to treat any patient having any galactosialidosis as encompassed by claim 9 without harming the patient is enormous and undue. Such experimentation entails searching and screening for any protein of any structure and function and determining whether any pharmaceutical composition comprising the protein would be useful in treating the patient having galactosialidosis without harming the patient.

The amount of experimentation to search for any pharmaceutical composition comprising any PPCA of any structure and function which can be used to treat any patient having any lysosomal storage disorder as encompassed by claim 10 without harming the patient is enormous and undue. Such experimentation entails determining whether a particular disease is a lysosomal storage disorder disease, determining the etiology of the disease, searching and screening for any PPCA protein of any structure and function, and determining whether any pharmaceutical composition comprising the PPCA protein would be useful in treating the patient having any lysosomal storage disorder without harming the patient.

Thus, searching for any of the claimed pharmaceutical compositions of claims 8-10 is well outside the realm of routine experimentation. Since such experimentation to make the pharmaceutical compositions encompassed by claims 8-10 is not routine in the art, where the expectation of obtaining any pharmaceutical composition comprising

any polypeptide of any structure and function which can be used to treat any patient having any lysosomal storage disorder is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the a specific protein composition which is effective in treating a patient having any lysosomal storage disorder. Without such a guidance, the experimentation left to those skilled in the art is undue. Claims 11-13 which depend from claim 8 are also rejected because they do not correct the defect of claim 8.

Claim Rejections - 35 U.S.C. § 102

Claims 8-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Sharp (WO 00/39150). The claims are product-by-process claims which are not limited by the manipulations of the recited steps. No patentable weight is give to the process where the claimed protein is produced in an insect cell culture (see MPEP § 2113). For examination purposes, the claims will only be examined as being directed to a pharmaceutical composition comprising a polypeptide useful for treating a lysosomal storage disorder.

Sharp discloses several nucleic acids and proteins encoded including TANGO 176 nucleic acids which encodes PPCA which can be used to treat galactosialidosis (see p. 27, line 19 to p. 28, line 6). Sharp teaches methods for production of the disclosed proteins including using insect cells (see pp. 67, lines 13-16). Sharp teaches

pharmaceutical compositions of the disclosed nucleic acids and proteins (see p. 72, line 19 to p. 76, line 9).

Thus, the reference teachings of Sharp anticipate the claimed invention.

(11) Response to Argument

35 U.S.C. § 112, 1st Paragraph - Written Description

Appellants assert beginning on page 5, 3rd paragraph, of the Brief that the proteins of the invention which may be included in the claimed composition are well known in the art and that the specification shows in Table 1 literature and/or Genbank accession numbers for the structure and amino acid sequence of these proteins. Appellants state that the structural information can be used in the recombinant expression of these proteins in any cell including insect cells. On page 6 of the Brief Appellants stated that the structures of the claimed proteins are well known in the prior art and that these structures are not required to be reproduced in the specification and are preferably omitted. To support this position Appellants cite the case *Hybridtech, Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

Appellants argue on page 6, 1st full paragraph, of the Brief that the amino acid sequence of the claimed proteins is not relied upon to impart patentability of the claimed composition and that the Appellants instead rely on the knowledge of the structures to supplement the aspects of the claimed invention. Appellants assert that recitation of the primary structure of each member of the proteins is not necessary and would be

redundant. On page 6, 2nd paragraph, of the Brief Appellants assert that the process for producing proteins in insect cells is straightforward and routine and thus may satisfy the written description requirement of the protein component of the claimed composition which is produced in insect cells.

Appellants argue on page 6, 3rd paragraph to page 7, 1st paragraph of the Brief that the proteins of the composition of claim 9 and 10 is listed on Table 1 of the specification, where claim 9 is limited to compositions for treating Galactosialidosis which is a lysosomal storage disorder associated with PPCA deficiency , and claim 10 is limited to PPCA. Appellants argue that the Examiner's assertion in the Final Rejection dated July 1, 2003, that the claims may encompass many proteins not listed in Table 1 of the specification, does not apply to claims 9 and 10. Appellants assert on page 7, 1st full paragraph, that a comprehensive list of lysosomal storage disorders (LSDs) and proteins are presented in Table 1 of the specification, that no LSDs or proteins other than those listed in Table 1 are known to exist, and that the Examiner has not identified any other LSDs and proteins.

Appellants argue on page 7, 2nd full paragraph, that Appellants' intent is to interpret the phrase "proteins useful for treating lysosomal storage disorders" in claim 8 and dependent claims to encompass the proteins and LSDs listed in Table 1 of the specification. Appellants assert that they have exercised the right to act as their own lexicographer and that this limits the scope of claim 8. In support of this position Appellants cite the case *Finnegan Corp. v. Int'l. Trade Comm 'n,* 180 F.3d 1354,1364, 51 U.S.P.Q. 2d 1001, 1008 (Fed. Cir. 1999).

Appellants argue on page 7,3rd full paragraph to page 8, that Appellants disagree with the accuracy of Examiner's assertion that "the specification does not provide a written description of administering any protein of any structure and function to treat any lysosomal storage disorder..." (Final Rejection at page 2, paragraph 5). Appellants assert that administration of the claimed compositions is sufficiently described with respect to the level of knowledge and skill in the art and at paragraphs 0065-0076 of Pub. No. 2002/0077292. Appellants state that the Examiner's assertion is not relevant to the question of whether the claimed compositions are sufficiently described.

Appellants' arguments have been fully considered but are not found to be persuasive to overcome the written description rejection for several reasons. MPEP §2111 states that claims must be given their broadest reasonable interpretation consistent with the specification and that such interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. The claims of the instant invention must be read in light of the specification to thereby interpret limitations explicitly recited in the claims. Thus, limitations of the specification cannot be read into the claims to narrow the scope of the claims by implicitly adding disclosed limitations which are not recited in the claims.

Thus, Appellants argument that claim 8 is to be interpreted and limited in scope to only encompassing the proteins and LSDs listed in Table 1 of the specification because Appellants desire to exercise their right to be their own lexicographer is not

persuasive since the disclosed limitations of Table 1 of the specification would be read into claim 8 and the disclosed limitations would be implicitly added to claim 8 to improperly limit the scope of claim 8.

Accordingly, the scope of genus claim 8, given the broadest reasonable interpretation consistent with the specification and consistent with the interpretation that those skilled in the art would reach, includes many proteins with widely differing structural, chemical, and physical characteristics which may be useful to treat lysosomal storage disorders that have widely differing etiologies based on their respective enzyme and/or protein deficiencies. The genus of proteins is highly variable because a significant number of structural differences between protein genus members is permitted. Furthermore, contrary to Appellants position, claims 8 and 9 encompass many other proteins not listed in Table 1 of the specification including proteins that can be found to be useful for just treating symptoms of any lysosomal storage disorder but not curing the lysosomal storage disorder, whether or not the protein directly replaces a deficiency or treats the symptoms of the lysosomal storage disorder.

For the same reasons stated above, the scope of genus claim 9 includes many proteins useful for treating Galactosialidosis where the proteins have widely differing structural, chemical, and physical characteristics. The scope of genus claim 10 includes many PPCA proteins with widely differing structural, chemical, and physical characteristics, and the genus is highly variable because a significant number of structural differences between PPCA protein genus members is permitted. Furthermore, the scope of genus claim 10 includes many widely differing lysosomal

storage disorders that have widely differing etiologies based on their respective enzyme and/or protein deficiencies.

Example 1 of the specification describes PPCA-deficient mouse macrophages taking in BV-neur and BV-PPCA resulting in the restoration of cathepsin A and neuraminidase activities in the PPCA-deficient mouse macrophages and treatment of PPCA-deficient mice with BV-neur and BV-PPCA resulting in a significant increase in the cathepsin A and neuraminidase activities in several systemic organs and the presence of PPCA in macrophages. Example 1 of the specification only shows one specific protein in a composition to treat one specific lysosomal storage disorder in mouse. However, the specification does not provide the specific amino acid sequence and structure of the BV-PPCA protein. Furthermore, the specification does not disclose any other examples of any other protein that is shown and demonstrated to be useful to treat any other lysosomal storage disorder. Instead the specification simply states in p. 14, line 30 to p. 15, line 10, how a subject suffering from sialidosis or GM1-gangliosidosis may be treated by administration of neuraminidase or beta-galactosidase, respectively. No information is provided which demonstrates that a subject suffering from sialidosis or GM1-gangliosidosis is successfully treated with neuraminidase or beta-galactosidase.

The specification and claims 8 and 9 do not indicate what distinguishing attributes are concisely shared by the protein members of the claimed genus which are desired to treat any lysosomal storage disorder which have widely differing etiologies based on their respective enzyme and/or protein deficiencies. The specification does

not clarify what common attributes are encompassed by the claimed genus of proteins of claims 8 and 9 useful for treating any lysosomal storage disorder. Concise structural features that could distinguish the proteins of the claimed genus from other proteins or compounds are missing from the disclosure. Furthermore, the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is needed.

The specification and claim 10 do not indicate what distinguishing attributes are concisely shared by any lysosomal storage disorder which can be treated with any PPCA protein of any structure and amino acid sequence, where the lysosomal storage disorders have widely differing etiologies based on their respective enzyme and/or protein deficiencies. The specification does not clarify what common attributes are encompassed by these lysosomal storage disorders which can be treated with any PPCA protein. While the Examiner agrees with Appellants' position that the process for recombinantly producing proteins in insect cells is routine in the art and that Table 1 of the specification lists several lysosomal storage disorders and protein/enzyme structures cited in the listed literature and Genbank accession numbers and that the structures of the cited proteins/enzymes are known in the prior art, the Examiner disagrees with Appellants' position that the specific amino acid sequence of the PPCA protein is not required to be disclosed in the specification and recited in claim 10. Claim 10 encompasses allelic variants of the PPCA protein which are not described by the specification where administration of such allelic variants of the PPCA protein may not be effective in treating any lysosomal storage disorder including galactosialidosis.

Given the lack of additional representative proteins useful for treating any lysosomal storage disorder and the specific amino acid sequence and structure of the PPCA protein of claim 10, Appellants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Appellants were in possession of the claimed invention. Claims 11-13 which depend from claim 8 are also rejected because they do not correct the defect of claim 8. Hence, claims 8-11 do not meet the written description requirement of 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, 1st Paragraph - Enablement

Appellants position on page 8, 3rd full paragraph, of the Brief is that as described in the response to the written description rejection, the invention is based on application of protein production process to known proteins, where the production process is straightforward and routine.

Beginning on page 9 of the Brief, Appellants argue that the examiner has not provided a basis for doubting the ability of a skilled artisan to produce the claimed pharmaceutical compositions. Appellants infers that the enablement rejection is based on the effectiveness and safety of the administration of the claimed compositions for treating lysosomal storage disorders, and that the rejection appears to be concerned with the utility of the administration of the claimed compositions rather than the ability to

make and administer these compositions. Appellants state that the claimed pharmaceutical compositions have specific, substantial, and credible utility where enzyme replacement therapy is used to treat lysosomal storage disorders. Appellants state that many proteins produced by processes other than production in insect cells have already been used or are being tested in clinical trials, where appellants cite paragraphs 0010-0034 of Pub. No. 2002/0077292.

Appellants argue on page 9, 2nd paragraph of the Brief that the Examiner's assertion that the amount of experimentation is undue and entails determining whether a disease is lysosomal disease, determining the etiology of the disease, and formulating a composition to treat or cure the disease cannot apply to claims 9 and 10. Appellants state that it is unclear why the rejection of claims 9 and 10 is sustained while the Final Rejection dated July 1, 2003, states that the specification is enabling for a composition comprising PPCA useful for treating galactosialidosis.

Beginning on page 10, 2nd full paragraph, Appellants argue that the scope of the claims is limited to proteins listed in Table 1 of the specification, where Table 1 shows an association between lysosomal storage disorders and proteins/enzymes deficient in each of the disorders. Appellants conclude that the practice of the claims does not entail determining whether a disease is a lysosomal storage disorder and determining the etiology of the disease since Appellants assert that this information is known and provided in Table 1.

Appellants state on page 10, 3rd full paragraph, that Appellants agree with the Examiner's position that the specification does not teach that any one protein/enzyme

can be used to treat every lysosomal storage disorder as encompassed by the claims. Appellants state that the specification teaches protein deficiencies associated with a particular lysosomal storage disorder and that the proteins can be made into pharmaceutical compositions to remedy the protein deficiency of the particular lysosomal storage disorder. Appellants do not agree that the claims encompass a single protein/enzyme for treating every lysosomal disorder since Appellants assert that the claims when read in light of the specification cover the use of a composition comprising alph-1,4 glucosidase and alpha-1,6 glucosidase to treat Pompe Disease.

On page 11, 1st full paragraph of the Brief Appellants state that the claimed pharmaceutical compositions have the same therapeutic uses as the prior art compositions containing protein produced by methods other than by insect cell production, and that the claimed compositions are enabled and are made using conventional insect cell expression techniques.

Appellants' arguments have been fully considered but are not found to be persuasive to overcome the scope of enablement rejection for several reasons. While the Examiner agrees with appellants' position that processes for producing proteins by expressing proteins in insect cells is routine to one skilled in the art of recombinant protein production, a pharmaceutical composition comprising a PPCA protein has utility for treating galactosialidosis, and that the scope of the claims does not encompass a single protein/enzyme for treating every lysosomal storage disorder, the Examiner

disagrees with appellants' position that the scope of the claims is limited to the proteins and lysosomal storage disorders listed in Table 1 of the specification.

MPEP §2111 states that claims must be given their broadest reasonable interpretation consistent with the specification and that such interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. The claims of the instant invention must be read in light of the specification to thereby interpret limitations explicitly recited in the claims. Thus, limitations of the specification cannot be read into the claims to narrow the scope of the claims by implicitly adding disclosed limitations which are not recited in the claims.

Thus, Appellants' argument that claim 8 is to be interpreted and limited in scope to only encompassing the proteins and lysosomal storage disorders listed in Table 1 of the specification is not persuasive since the disclosed limitations of Table 1 of the specification would be read into claim 8 and the disclosed limitations would be implicitly added to claim 8 to improperly limit the scope of claim 8.

Accordingly, claim 8 encompasses any pharmaceutical composition comprising any pharmaceutically acceptable carrier and any protein of any structure and function useful for treating any lysosomal storage disorder other than Fabry disease, wherein the claimed protein is selectively imported into macrophages when administered to a subject and the protein is produced in any insect cell.

Appellants' arguments that undue amount of experimentation to make the claimed pharmaceutical composition of claim 8 is not required is not found persuasive. The amount of experimentation to search for any pharmaceutical composition

comprising any protein of any structure and function which can be used to treat any patient having any lysosomal storage disorder as encompassed by claim 8 without harming the patient entails performing tests on a patient to determine and confirm whether a patient has any lysosomal storage disorder, ascertaining the etiology of the disease which may or may not be directly known , searching and screening for any protein of any structure and function, and determining whether any pharmaceutical composition comprising the protein would be useful in treating the patient having any lysosomal storage disorder without harming the patient.

The Examiner's position is that teachings regarding searching or screening for proteins/enzymes useful for treating any lysosomal storage disorders is not guidance for making the claimed pharmaceutical composition comprising any protein of any structure and function which can be used to treat any patient having any lysosomal storage disorder as encompassed by claim 8.

It cannot be predicted whether any protein of any structure and function can be used to treat any patient having any lysosomal storage disorder without any harming the patient. The specification does not disclose any other examples of any other protein that is shown and demonstrated to be useful to treat any other lysosomal storage disorder other than the BV-neur and BV-PPCA used in Example 1 of the specification. Instead the specification simply states how a subject suffering from sialidosis or GM1-gangliodsidosis may be treated by administration of neuraminidase or beta-galactosidase, respectively (see p. 14, line 30 to p. 15, line 10 of the specification). No

information is provided which demonstrates that a subject suffering from sialidosis or GM1-gangliodsidosis is successfully treated with neuraminidase or beta-galactosidase.

Appellants' arguments that the enablement rejection cannot apply to claims 9 and 10 are not persuasive since each of claims 9 and 10 do not recite the limitations of a composition comprising PPCA useful for treating galactosialidosis. Claim 9 encompasses any pharmaceutical composition comprising any protein of any structure and function useful for treating galactosialidosis while claim 10 encompasses any pharmaceutical composition comprising any PPCA protein of any structure and amino acid sequence useful for treating any lysosomal storage disorder.

The amount of experimentation to make the pharmaceutical composition as encompassed by claim 9 is undue and entails searching and screening for any protein of any structure and function and determining whether any pharmaceutical composition comprising the protein would be useful in treating the patient having galactosialidosis without harming the patient. The amount of experimentation to make the pharmaceutical composition as encompassed by claim 10 is undue and entails determining whether a particular disease is a lysosomal storage disorder, determining the etiology of the disease, searching and screening for any PPCA protein of any structure and function, and determining whether any pharmaceutical composition comprising the PPCA protein would be useful in treating the patient having any lysosomal storage disorder without harming the patient.

Since such undue experimentation to make the pharmaceutical compositions encompassed by claims 8-10 is not routine in the art, where the expectation of obtaining

any pharmaceutical composition comprising any polypeptide of any structure and function which can be used to treat any patient having any lysosomal storage disorder is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the a specific protein composition which is effective in treating a patient having any lysosomal storage disorder. Without such a guidance, the experimentation left to those skilled in the art is undue. Claims 11-13 which depend from claim 8 are also rejected because they do not correct the defect of claim 8. Hence, claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for composition comprising a PPCA protein useful for treating galactosialidosis, does not reasonably provide enablement for any other embodiment.

Claim Rejections - 35 U.S.C. § 102

Appellants state on page 11, 3rd full paragraph of the Brief that the Examiner asserts that the Sharp reference does not teach a pharmaceutical composition comprising a PPCA protein produced in an insect cell culture and that a teaching for production of PPCA in insect cell culture is not necessary to anticipate the claimed invention since the claims do not recite properties associated with proteins produced in insect cells which could distinguish them from proteins from other means. Appellants conclude that the requirement for the recitation of properties of a product in a product by process claim in order for those properties to be considered for determining patentability over the prior art is wrong.

Beginning on page 11, 4th full paragraph of the Brief Appellants assert that patentability of product by process claims depends on the presence or absence of characteristics and properties of the product produced by the recited process and does not depend on the patentability of the recited process. In support of Appellants' position, appellants cite MPEP Section 2113 and the cases of *In re Pilkington*, 411 F2d 1345; 162 U.S.P.Q. 145 (C.C.P.A. 1969); and *In re Thorpe*, 777 F.2d 695, 697, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985)

Appellants argue on page 11, 2nd full paragraph of the Brief that the specification has described the unique characteristics of proteins produced in insect cells, specifically, their glycosylation pattern and exposed mannose residues. Appellants assert that the unique characteristics of proteins produced in insect cells do not fit into the form of a claim limitation and appellants thus used the product by process claim format for this situation.

Beginning on page 12, 1st paragraph, Appellants argue that by taking the unique characteristics of proteins produced in insect cells into account then the Sharp reference does not anticipate the claimed invention. Appellants state that the Sharp reference generically mentions production of protein in insect cells and host cells that may be used for producing proteins (see Sharp pp. 65-72, especially pp.65-67). Appellants argue that the Sharp reference does not specifically teach production of PPCA (i.e. TANGO 176 protein) in insect cell culture useful for treating galactosialidosis. Appellants' position is that no teaching can be inferred from the Sharp reference that the

TANGO 176 protein can be useful for treating galactosialidosis when considering the state of the art at the time of the Sharp disclosure.

Appellants' position is that the specification teaches that there are difference between the post-translational modification of proteins in insect cells and mammalian cells and that the post-translational modification of proteins in insect cells are not well defined. Appellants assert that the ill-defined nature of post-translational modification of proteins in insect cells is considered a disadvantage for protein production in insect cells.

Appellants conclude that in view of the sate of the art at the time of filing of the application the Sharp reference would not teach the skilled artisan the concept of producing PPCA in an insect cell for producing a pharmaceutical composition for treating galactosialidosis and that this concept is only apparent from Appellants' disclosure.

Appellants' arguments have been fully considered but are not found to be persuasive to overcome the rejection for several reasons.

MPEP §2113 states:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product

of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

MPEP §2112 states:

"The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)."

On page 14, lines 23-29 of the specification, Appellants cite the reference of Hahn et al. [Proc. Natl. Acad. Sci. 95: 14880-14885 (1998)] which teaches that transgenic PPCA-deficient mice transplanted with bone marrow from transgenic mice overexpressing PPCA resulted in a correction of the systemic pathology in the transgenic PPCA-deficient mice. Since the Hahn et al. reference was published prior to the publication date of the Sharp reference, one skilled in the art at the time of the publication of Sharp would known that administering PPCA can treat galactosialidosis, where galactosialidosis is associated with a deficiency of PPCA.

Sharp discloses several nucleic acids and proteins encoded including TANGO 176 nucleic acids which encodes PPCA which can be used to treat galactosialidosis (see p. 27, line 19 to p. 28, line 6). Sharp teaches methods for production of the disclosed proteins including using insect cells (see pp. 67, lines 13-16). Sharp teaches

pharmaceutical compositions of the disclosed nucleic acids and proteins (see p. 72, line 19 to p. 76, line 9).

Although Sharp provides no explicit examples of a pharmaceutical composition comprising a PPCA protein useful for treating galactosialidosis, the skilled artisan would concluded, in view of the teachings of Hahn et al. [Proc. Natl. Acad. Sci. 95: 14880-14885 (1998)] and MPEP §2112 and MPEP §2113, that Sharp was in possession of a pharmaceutical composition comprising a PPCA protein which is expected to be useful for treating galactosialidosis.

Since Sharp teaches that TANGO 176 nucleic acids which encode PPCA can be expressed and produced in insect cells thereby resulting in a PPCA having the post-translational modifications including glycosylation pattern and exposed mannose residues associated with production of proteins in insect cells, then such PPCA product is expected to inherently have the same characteristics and properties of the claimed PPCA protein produced in insect cells as encompassed by claims 8-13.

Thus, the skilled artisan would conclude that the teachings of Sharp anticipate Appellants' invention. Hence, claims 8-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Sharp (WO 00/39150).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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